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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,708	01/14/2004	Derek O' Hagan	PP-19768.002	3852

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EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/757,708	O' HAGAN ET AL.	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,32-39,42-48,52,54-64,69 and 72-101* is/are pending in the application.

4a) Of the above claim(s) *see continuation sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26-28, 34-39, 42-48, 52, 54-57, 61, 63, 64, 69, 76-79, 86, and 90-101* _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-28,32-39,42-48,52,54-64, 69,72-101.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 4,7,11,14,19-22,24,25,32,33,58-60,62,72-75,80-85 and 87-89.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/21/2007 has been entered.

Election/Restrictions

2. A restriction requirement between the different inventions and species recited in the claims was mailed on 03/10/2006. Applicant responded by electing the invention of Group II, drawn to microparticles comprising a biodegradable polymer, a surfactant, a polynucleotide and an adjuvant adsorbed on the microparticle; the reply was filed on 05/10/2006.

Upon further consideration, the inventions of Groups IV (claims 56, 63, and 64) and V (claims 57, 63, and 64) are hereby rejoined and examined together with the elected invention. It is noted that the search for the invention of Group II yielded results relevant for the inventions of Groups IV and V. Therefore, examining these three inventions together does not constitute a burden for the Examiner. Similarly, claim 43, drawn to the non-elected species of Th1 response is hereby rejoined.

Claims 29-31, 40, 41, 49-51, 53, 65-68, 70, and 71 have been cancelled. Claims 4, 7, 11, 14, 19-22, 24, 25, 32, 33, 58-60, 62, 72-75, 80-85, and 87-89 have been withdrawn. Claims 90-101 are new. Claims 1 and 52 have been amended.

Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26-28, 34-39, 42-48, 52, 54-57, 61, 63, 64, 69, 76-79, 86, and 90-101 are under examination.

3. All rejections pertaining to claims 31 and 53 are moot because Applicant cancelled the claims in the response filed on 11/21/2007.

The provisional rejection of claim 52 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 13 of the U.S. Application No. 11/113,861 is withdrawn because Applicant withdrew claim 13 in Application No. 11/113,861.

The rejection of claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 27, 28, 34-39, 42, 44-48, 52, 54, 55, 61, and 69 under 35 U.S.C. 103(a) as being unpatentable over Singh et al. (Proc Natl Acad Sci USA, 2000, 97: 811-816) is withdrawn in response to Applicant's amendments to the claims filed on 11/21/2007.

Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 27-31, 34-39, 42, 44-48, 52-55, 61, 69, and 76-79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al. in view of both Thalhamer et al. (Endocrine Regulations, 2001, 35: 143-166) and Diwan et al. (Journal of Controlled Release, 2002, 85: 247-262) is withdrawn in response to Applicant's amendments to the claims filed on 11/21/2007.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude"

A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26-28, 34-39, 42-48, 52, 54, 55, 61, 69, 76-79, and 90-101 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5-19, 24-26, and 35-40 of U.S. Patent No. 6,884,435. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are obvious variants.

The instant claims are drawn to **(i)** microparticles comprising a biodegradable polymer, a cationic lipid, and a first polynucleotide-containing species adsorbed on the surface of the microparticles, wherein the first polynucleotide species constitute at least 5% of the total weight of the microparticles, the cationic surfactant is

cetyltrimethylammonium bromide (CTAB), the biodegradable polymer is poly(lactide-co-glycolide) (PLG), the first polynucleotide-containing species encodes for an antigen derived from a pathogenic organism such as HIV, the microparticles further comprise an immunological adjuvant such as CpG ; the microparticles can contain 01-10 wt% cationic surfactant or additional microparticles comprising entrapped or adsorbed immunological adjuvants (claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26-28, 34-37, 43, 69, 76-79, and 90, 91, and 96-100), **(ii)** a method of producing the microparticles by obtaining a w/o/w emulsion comprising the polymer and the surfactant, removing the organic solvent from the solution and adsorbing the first polynucleotide-containing species to the microparticles (claims 52, 54, 55, 92-95, and 101), **(iii)** a method of delivering a therapeutic amount of polynucleotide to a host animal (claim 38), and **(iv)** a method of stimulating an immune response, wherein the immune response comprises a CTL immune response (claims 39, 42, 44-48).

The patent claims recite **(i)** a microparticle comprising a polymer such as PLG, a cationic detergent such as CTAB, and an antigen comprising a polynucleotide such as plasmid (example 7 discloses that the plasmid is pCMV) adsorbed on the surface of the microparticle, wherein the polynucleotide encodes for an antigen derived from a pathogenic organism such as HIV and wherein the microparticle is formed in the presence of the detergent and then exposed to the polynucleotide (the specification defines that a w/o/w solvent evaporation system can be used to form the microparticles, see column 13, lines 10-39); the microparticles further comprise CpG as an immunological adjuvant (claims 1, 5-13, 16, 17, 19, 20, 24-26, 35-37) and **(ii)** a method

for raising an immune response by administering the microparticles to a vertebrate animal (the specification discloses that the intent of delivery is to use the particle as a vaccine to elicit an immune response in a vertebrate and to treat a disease, see column 4, lines 3-30; additionally the specification defines that a vertebrate can be a human, column 8, lines 45-52) (claims 38-40). The specification discloses that the polynucleotide can constitute 5% or 0.1 to 10% of the total weight of the microparticle (column 14, lines 6-10) and that the microparticles comprise 0.1 to 10% or 0.5 to 2 % cationic surfactant (column 13, lines 30-37). The specification also discloses that the cataionic surfactant is not removed after the formation of the microparticles (column 13, lines 10-39). With respect to the limitation of the adjuvant being adsorbed on the surface of the microparticle, the specification discloses that adjuvants can be used to enhance the immunogenicity of the microparticles and that the adjuvants can be adsorbed on the microparticles (column 14, lines 36-51). With respect to the limitation recited in claim 3, the specification discloses that the microparticles have a diameter of about 200 nm to about 30 μm that includes the range recited by claim 3 (column 5, lines 1-10). With respect to the limitation of the polynucleotide constituting 10-20% of the total microparticle weight (the instant claims 27, 28, , 91, and 93), it would have been obvious to one of skill in the art to adjust the amount of delivered polynucleotide according to particular needs by varying the amount of adsorbed polynucleotide. It is routine in the art to vary the relative ratios of the microparticle components and test for the combinations that result in better activity.

Thus, the patent claims 1, 5-19, 24-26, and 35-40 anticipate claims 1-3, 5, 6, 8-

10, 12, 13, 15-18, 23, 26-28, 34-39, 42-48, 52, 54, 55, 61, 69, 76-79, and 90-101 of the instant application. Since the US Patent No. 6,884,435 claims 1, 5-19, 24-26, and 35-40 embrace all limitation of the instant claims the patent claims and the instant claim are obvious variants of one another.

Applicant argues that the patent specification can be used as a dictionary to learn the meaning of a term in the claim; the specification cannot be used as prior art in an obviousness-type double patenting rejection (MPEP 804). Applicant argues that the specification of the '435 patent defines the term "microparticles" as being a particle about 100 nm to 150 μm in diameter (column 5, lines 1-10), without mentioning the amount of macromolecules and detergent that must be present in a particle in order to be termed a "microparticle". Applicant submits that the Examiner used the patent specification to provide missing claim limitations, i.e., as prior art, which is impermissible in conjunction with an obviousness-type double patenting rejection.

Applicant's arguments are acknowledged, however, they are not found persuasive for the following reasons:

The patent specification was used to define the microparticle characteristics (and not only the term "microparticle) in order to determine whether the claimed invention is an obvious variation of the invention claimed in the '435 patent. In doing this, the Examiner used only those portions of the specification pertaining to the invention claimed in the patent. Therefore, the rejection is maintained.

The following is a citation from MPEP 804 [R-5] II B:

Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. In re Vogel, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970). The court in Vogel recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court, one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined.

6. Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26, 28, 34-37, 54, 55, 61, 69, 76-79, and 90-101 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5, 11, 30, 31, 36, 37, 40, 43, 45-47, 58, 59, 79, and 71 of the U.S. Application No. 11/113,861. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are obvious variants.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The instant claims are drawn to **(i)** microparticles comprising a biodegradable polymer, a cationic lipid, and a first polynucleotide-containing species adsorbed on the surface of the microparticles, wherein the first polynucleotide species constitute at least 5% of the total weight of the microparticles, the cationic surfactant is cetyltrimethylammonium bromide (CTAB), the biodegradable polymer is poly(lactide-co-

glycolide) (PLG), the first polynucleotide-containing species encodes for an antigen derived from a pathogenic organism such as HIV, the microparticles further comprise an adsorbed immunological adjuvant such as CpG and can contain 01-10wt% cationic surfactant (claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26, 29, 30, 34-37, 69, 76-79, 86, and 90, 91, and 96-100), **(ii)** a method of producing the microparticles by obtaining a w/o/w emulsion comprising the polymer and the surfactant, removing the organic solvent from the solution and adsorbing the first polynucleotide-containing species to the microparticles (claims 52, 54, 55, 92-95, and 101), **(iii)** a method of delivering a therapeutic amount of polynucleotide to a host animal (claim 38), and **(iv)** a method of stimulating an immune response, wherein the immune response comprises a CTL immune response (claims 39, 42, 44-48).

The application claims recite a microparticle comprising a biodegradable polymer such as PLG, a cationic detergent, an immunological adjuvant and an antigen derived from a pathogenic organism such as HIV, wherein both the immunological adjuvant and the antigen are adsorbed on the surface of the microparticle, wherein the biodegradable polymer is PLG, and wherein the microparticles are formulated into an injectable pharmaceutical composition (claims 1-5, 11, 30, 31, 40, 43, 45-47,58, 59, 70, and 71); the adjuvant comprises CpGs (claims 36 and 37). The specification discloses that the antigen can be a plasmid such as pCMV encoding gp120 and that the cationic surfactant can be CTAB (p. 1, paragraph 0002, p. 4-5, paragraph 0019, p. 7, paragraph 0037, p. 17, paragraph 0070, Example 7). With respect to the limitation of the size of the particles being between 200 nm and 20 μm, the specification discloses that the

microparticles can have a diameter of 200 nm to 30μm. The specification also discloses that the polynucleotide can constitute 5% or 0.1 to 10% of the total weight of the microparticle (p. 8, column 1, paragraph 0091) and that the microparticles comprise 0.1-10% or 0.5-2 % or cationic surfactant, wherein microparticle can comprise 1% detergent relative to the biodegradable polymer, and that the microparticles are obtained without removal of the detergent after particle formation (p. 18-19, paragraph 0075).

Thus, the application claims 1-5, 11, 30, 31, 36, 37, 40, 43, 45-4758, 59, 79, and 71 anticipate claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26, 28, 34-37, 52, 54, 55, 61, 69, 76-79, 86, and 90-101 of the instant application. Since the US Application No. 11/113,861 claims 1-5, 8, 10, 11, 13, 15-21, 24-27, 30, and 31 embrace all limitation of the instant claims, the patent claims and the instant claim are obvious variants of one another.

Applicant argues that Application No. 11/113,861 is a continuation of Application No. 09/581,772, which matured as the U.S. Patent No. 6,884,435 and therefore, the arguments set forth above are applicable to the provisional double patenting as well.

The rejection is maintained for the reasons stated above.

35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26-28, 34-39, 42-48, 52, 54-57, 61, 63, 64, 69, 76-79, 86, and 90-101 are rejected under 35 U.S.C. 102(e) as being anticipated by O'Hagan et al. (U.S. Patent No. 6,884,435, of record), as evidenced by Thalhamer et al. (Endocrine Regulations, 2001, 35: 143-166).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

O'Hagan et al. teach a microparticle comprising a biodegradable polymer such as PLG, a cationic surfactant such as CTAB, and a polynucleotide adsorbed on the surface of the microparticle (claims 1-3, 5, 6, 90, and 100), wherein the microparticles have a diameter of 200 nm to 30 μm, wherein the polynucleotide constitutes at least 5% or 10% of the total weight of the microparticle, wherein the polynucleotide is a plasmid such as pCMV (i.e., comprising CpGs) and wherein the plasmid encodes an antigen derived from a pathogenic organism such as HIV gp120 (claims 1, 8-10, 12, 13, 15-18, 27, 28, 61, 69, 90, 91, and 100); the microparticle is formed in the presence of the

cationic surfactant and the cationic surfactant is not removed after the formation of the microparticle and contains at least 5% (claim 1) (Abstract, column 2, lines 37-67, column 3, lines 17-34, column 5, lines 1-5, 28-35, and 65-67, column 9, lines 5-15, column 11, lines 1-6, column 12, lines 6-19, column 14, lines 1-12, Examples 2 and 7). O'Hagan et al. teach that the microparticles can be formulated into an injectable pharmaceutical composition, wherein the pharmaceutical composition further comprises an adjuvant such as an aluminum salt and wherein the adjuvant is adsorbed on the microparticle (claims 23, 26, 34-37, 55, 76-79) (column 14, lines 36-67, column 15, lines 66 and 67). O'Hagan et al. also teach a method of producing the above microparticle by forming a w/o/w emulsion comprising the cationic surfactant and the biodegradable polymer at a weight to weight ratio of 0.01:1, followed by the removal of the organic solvent and the absorption of the polynucleotide (claims 52, 54, and 92-95) (column 13, lines 10-39). In addition to the above, O'Hagan et al. teach a method for raising an immune response by administering their microparticles to a human (claims 38, 39, and 45-48), wherein the immune response comprises a CTL response (claims 42 and 44) (column 4, lines 3-30, column 7, lines 25-35, column 8, lines 45-52). With respect to claims 27, 28, 91, and 93, O'Hagan et al. teach that the polynucleotide can constitute 0.1% to 10% of the total weight of the microparticle (column 14, lines 8 and 9); the value of 10% is the same as the claimed lower point of the claimed range, and therefore, O'Hagan et al. anticipate the range 10% to 20% or 10% to 30% recited in claims 27, 28, 91, and 93. With respect to the limitation of the microparticle comprising 0.1 to 10 wt% cationic surfactant (claim 96), O'Hagan et al. teach a weight to weight ratio of cationic

surfactant to polymer of 0.001:1, i.e., the microparticle comprises 0.1% cationic surfactant (column 13, lines 30-37). With respect to the limitation of the microparticles comprising 0.5 to 2 % cationic surfactant (claims 97 and 101), O'Hagan et al. teach a weight to weight ratio of cationic surfactant to polymer of 0.005 to 1, i.e., the microparticle comprises 0.5% cationic surfactant (column 13, lines 30-37). With respect to the limitations recited in claims 98 and 99, O'Hagan et al. teach a ratio of cationic surfactant to biodegradable polymer of 0.01:1, i.e., the amount of surfactant is 1% relative to the biodegradable polymer (column 13, lines 30-37). With respect to the limitation recited in claims 56, 63, 64, and 86, O'Hagan et al. teach that the microparticle composition can comprise additional microparticles with the adjuvant adsorbed on their surface (column 14, lines 35-51); with respect to the limitation of the microparticles further comprising an immunological adjuvant (claim 64), it is noted that the microparticles of O'Hagan et al. comprising adsorbed plasmid contain CpGs, i.e., they further contain an immunological adjuvant. With respect to the limitations recited in claim 57, O'Hagan et al. teach that the microparticle composition can comprise additional microparticles with entrapped adjuvant (column 14, lines 35-51). With respect to the limitation of microparticle eliciting a Th1 response (claim 43), it is noted that this is an inherent property of CpGs (see Thalhamer et al., p. 145, column 2); since the microparticles of O'Hagan et al. comprise CpGs, they must necessarily induce a Th1 immune response.

Since O'Hagan et al. teach all the claim limitations, the claimed invention is anticipated by the above-cited art.

Applicant argues that the ranges disclosed by O'Hagan et al. are not specific to constitute anticipation under the statute and case law and that the present case is analogous to *Atofina v. Great Lakes Chem Corp,* 441 F.3d 991, 999, 78 USPQ2d 1417, 1423 (Fed. Cir. 2006), in which case the court held that a reference describing a temperature range of 100-500° C did not describe the claimed range of 330-450° C. Applicant submits that, with respect to the narrow range disclosed by O'Hagan et al. (i.e., microparticles with adsorbed macromolecule having a weight to weight ratio of 0.01 to 0.05), there is no overlap between the ranges of the instant claims 27, 28, 52, 91, and 93 and only the end point of claim 1 appears to touch this range. Applicant points out that Example 7 in O'Hagan et al. describes pCMV loads ranging from 0.84 to 2.36% with decreasing loading efficiencies ranging from 88% to 59%, i.e., the loading efficiency decreases with increasing target load. Therefore, Applicant argues, O'Hagan et al. do not anticipate claims 1, 27, 28, 52, 91, and 93 and their dependent claims because the claimed amounts of adsorbed polynucleotide are not disclosed with sufficient specificity to constitute anticipation of the claims. With respect to the cationic detergent, Applicant argues that the ranges taught by O'Hagan et al. (column 13, lines 32-37) pertain to detergents in general, which are defined as including surfactants and emulsion stabilizers (column 5, lines 28-36), wherein the ranges are not specific enough to constitute anticipation. Applicant points out that Example 2 of O'Hagan et al. teaches a CTAB to polymer ratio of 0.5:1 (i.e., 50% CTAB relative to polymer), much higher than the range recited in claim 52, while Example 1 of the instant specification discloses 1% and 4% CTAB relative to polymer; however the particles in Example 2 are washed four

times resulting in CTAB removal, which is in contrast to the claimed invention wherein the particles are not washed and the amount of detergent in microparticles is the same as the amount used to form the particles. Applicant argues that it is not obvious to eliminate the cationic surfactant removal step as claimed, because, as indicated by Singh (p. 815, column 2, third paragraph) there is a strong incentive to keep CTAB levels to a minimum. Applicant submits that the claimed microparticles with the levels of cationic surfactant as recited in claims 97, 100, and 101 were unexpectedly found to exhibit enhanced immunogenicity, not only relative to the naked DNA, but also to microparticle having higher amounts of cationic surfactant, which is surprising given the higher loading efficiencies (and thus, higher loadings) observed with the higher amounts of cationic surfactants. For these reasons, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, they are not found persuasive for the following reasons:

Applicant's argument that the broad range of polynucleotide amounts disclosed by O'Hagan et al. (i.e., 0.0001:1 to 0.25:1) does not anticipate the claimed values is not found persuasive because O'Hagan et al. clearly teach narrower ranges, wherein the narrower ranges provide specific examples falling within the claimed ranges. With respect to claim 1, O'Hagan et al. teach that the polynucleotide can constitute 1% to 5% of the total weight of the microparticle (column 14, line 9); the value of 5% is the same as the claimed value, and therefore, O'Hagan et al. anticipate the limitation of the polynucleotide constituting at least 5% as recited in claim 1. With respect to claims 27,

28, 91, and 93, O'Hagan et al. teach that the polynucleotide can constitute 0.1% to 10% of the total weight of the microparticle (column 14, lines 8 and 9); the value of 10% is the same as the claimed lower point of the claimed range, and therefore, O'Hagan et al. anticipate the limitation of the polynucleotide constituting 10% to 20% or 10% to 30% of the total weight of the microparticle as recited in claims 27, 28, 91, and 93. Therefore, the instant case is not similar to *Atofina*, because in *Atofina*, while the prior art disclosed a range touching the claimed range, no specific example falling within the claimed range were given. In the instant case, the claimed ranges are disclosed with specificity by O'Hagan et al. (specific examples are given), and therefore, O'Hagan et al. anticipates the claims. The following is a citation from MPEP:

> 2131.03 [R-6] Anticipation of Ranges
>
> I. A SPECIFIC EXAMPLE IN THE PRIOR ART WHICH IS WITHIN A CLAIMED RANGE ANTICIPATES THE RANGE
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> "[W]hen, as by a recitation of ranges or otherwise, a claim covers several compositions,the claim is anticipated' if one of them is in the prior art." Titanium Metals Corp. v.Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) (citing In re Petering, 301 F.2d 676, 682, 133 USPQ 275, 280 (CCPA 1962)) (emphasis in original) (Claims to titanium (Ti) alloy with 0.6-0.9% nickel (Ni) and 0.2-0.4% molybdenum (Mo) were held anticipated by a graph in a Russian article on Ti-Mo-Ni alloys because the graph contained an actual data point corresponding to a Ti alloy containing 0.25% Mo and 0.75% Ni and this composition was within the claimed range of compositions).

The same considerations apply to the ranges of cationic surfactant (claims 97-99 and 101). With respect to claim 96, O'Hagan et al. teach a weight to weight ratio of cationic surfactant to polymer of 0.001:1 (column 13, line 35), i.e., the microparticle comprises 0.1% cationic surfactant, which anticipates the limitation of the microparticle

comprising 0.1 to 10 wt% cationic surfactant recited in the claim. With respect to claims 97 and 101, O'Hagan et al. teach a weight to weight ratio of cationic surfactant to polymer of 0.005 to 1 (column 13, line 36), i.e., the microparticle comprises 0.5% cationic surfactant (column 13, lines 30-37), which anticipates the range of 0.5 to 2 % recited in claims 97 and 101. With respect to claims 98 and 99, O'Hagan et al. teach a ratio of cationic surfactant to biodegradable polymer of 0.01:1 (column 13, line 37), i.e., the amount of surfactant is 1% relative to the biodegradable polymer, which anticipates the limitation recited in the claims. With respect to claim 52, O'Hagan et al. teach cationic surfactant and the biodegradable polymer at weight to weight ratios of 0.01:1 (column 13, line 34), range which falls within and therefore anticipates the claimed range of 0.0025: to 0.05:1.

With respect to Example 7, Applicant argues that the loading efficiency decreases with increasing the target load, as demonstrated in Table IV. While this is true, it is noted that Table IV clearly indicates that increasing the amount of DNA results in higher amounts of adsorbed DNA, even if the loading efficiency decreases (compare the theoretical loads with the actual load for the PLG-CTAB particles). Therefore, one of skill in the art would know to achieve the desired loading by increasing the amount of DNA to be adsorbed. However, regardless of what Example 7 discloses, the teachings of O'Hagan et al. anticipate the claimed invention, since the specification teaches the claimed ranges with specificity, as indicated above.

With respect to Example 2, it is noted that this is only one embodiment. O'Hagan et al. clearly teach obtaining microparticles without washing (column 13, lines 10-39 and

column 14, lines 1-12).

The argument of unexpected results is irrelevant to an anticipation rejection and cannot overcome a rejection (see MPEP 2131.04).

For all the reasons above, the rejection is maintained.

9. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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